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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,361	10/31/2003	Czeslaw Radziejewski	REG 930A	3038

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EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,361	RADZIEJEWSKI ET AL.	
	Examiner	Art Unit	
	Leon Y Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040823*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-16, drawn to a method of identifying a site of interaction, classified in class 435, subclass 7.1.

   II. Claims 17-21, drawn to a method of sorting antigen-specific monoclonal antibodies, classified in class 436, subclass 518.

2. The inventions are distinct, each from the other because of the following reasons:

3. Inventions I and II are unrelated, independent, and distinct. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, different functions, and different effects. Group I is a method of identifying a site of interaction between a first and second macromolecule, which is a different effect from Group II, which has the effect of sorting antigen-specific monoclonal antibodies (mAbs) into functional groups. Group I also includes the step of identifying a site of interaction between the first and second macromolecules based on the interaction profile, which is not a step in Group II. Group II also includes the step of

sorting the mAbs into functional groups based on a binding profile of the monoclonal antibodies to each treated biosensor surface, wherein mAbs that exhibit similar binding profiles to each treated sensor are sorted into the same functional group, which is not a step in Group I.

Therefore, Groups I and II have different modes of operation, different functions, and different effects that distinguish them as unrelated, independent, and distinct inventions.

4. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Valeta Gregg on 23 August 2004 a provisional election was made without traverse to prosecute the invention of Group II, claims 17-21. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

7. In claim 17, line 1, the term "antigen-specific monoclonal antibodies (mAbs)" is vague and indefinite. Although the definition of a mAb is clear, it is unclear whether more than one type of mAb is claimed. If only one type of mAb is claimed, then it is confusing as to how the mAb can be separated into "functional groups" (lines 1 and 9).

8. In claim 17, lines 4-5, the phrase "is capable of altering the structure of the immobilized antigen" is vague and indefinite. The specification does not provide a definition for the phrase and it is unclear whether the structure of the immobilized antigen is altered. Does the agent actually alter the immobilized antigen or does it just has the ability to do so? Also, how is the structure altered? Is the alteration chemical, physical, or by another method? Applicant is invited to clarify the limitation.

9. In claim 17, line 5, the term "structure" is vague and indefinite. The specification does not provide a definition for the term and it is unclear what part of the antigen structure is altered. Is a specific epitope altered or just one molecule? Applicant is invited to clarify the limitation.

10. In claim 17, line 9, the term "sorting" is vague and indefinite. The specification does not provide a definition for the term and it is unclear as to how the mAbs are being sorted. It the sorting a physical grouping of the mAbs or is the separation of mAbs by another method? Applicant is invited to clarify the limitation.

11. Claim 1 recites the limitation "the antigen" in line 3. There is insufficient antecedent basis for this limitation in the claim.

12. Claim 21 contains the trademark/trade names Biacore, IAsys, SPR670, Bio-Suplar II, and Spreeta. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a biosensor surface and, accordingly, the identification/description is indefinite.

Specification

13. The use of the trademarks Biacore, IAsys, SPR670, Bio-Suplar II, and Spreeta have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Colyer et al (WO 00/50902) in view of Pfund et al (Molecular Immunology 1990, 27(6):495-502).

Colyer et al reference teaches a method comprising immobilizing the antigen onto at least two biosensor surfaces, treating each biosensor surface with a different agent, wherein each agent is capable of altering the structure of the immobilized antigen, exposing each treated biosensor surface to antibodies, and determining the binding profile of the antibodies to each treated biosensor surface, by disclosing one or more immobilized polypeptides, wherein at least one of the immobilizes polypeptides is susceptible to modification, said modification being detectable by a method comprising contacting the immobilized peptide with a test sample which may contain an agent capable of modifying the immobilized polypeptide, contacting the immobilized

polypeptide with a binding partner polypeptide wherein the binding of this partner polypeptide to the immobilized polypeptide is at least partly dependent on the modification state of the immobilized polypeptide, and measuring the association of the binding partner polypeptide to the immobilized polypeptide (page 6, lines 14-24), wherein a polypeptide is susceptible to "modification" if it is capable of serving as a substrate for one or more modifying enzymes or one or more chemical agents(s), either singly or in combination (page 8, lines 30-32 and page 9, lines 7-8), wherein peptide or protein substrates peculiar to different enzymes can be immobilized to discrete areas of the same physical support, thereby providing a means of examining the activity of a number of enzymes from the same sample in parallel (page 20, lines 8-10 and Figure 17).

However, Colyer et al reference fails to teach that the binding partner polypeptides are monoclonal antibodies (mAbs) and also fails to teach the step of sorting the mAbs into functional groups based on a binding profile of the monoclonal antibodies to teach treated biosensor surface, wherein mAbs that exhibit similar binding profiles to each treated sensor surface are sorted into the same functional group.

Pfund et al reference teaches monoclonal antibodies Anti-bSt-1 through Anti-bSt-4, Anti-bSt-7, and Anti-bSt-16 to bovine somatotropin (bSt), wherein the six monoclonal antibodies have been characterized and grouped, wherein three of these antibodies (Anti-bSt-1,2, and 3) demonstrate strong reactivity with native AIM-bound bSt but little or no reactivity with conformationally modified bSt, Anti-bSt-4 is capable of recognizing all forms of bSt examined, Anti-bSt-7 binds well to native bSt and to bSt denatured under

non-reducing conditions, and Anti-bSt-16 is "conformation-sensitive", in order to determine the reactivities of antibodies with native and conformationally modified antigenic species that may be evaluated side-by-side (page 496, left column, 1st paragraph, lines 15-18 and right column, 2nd paragraph, lines 1-3; page 500, right column, 3rd-5th paragraphs; page 501, left column, 1st-2nd paragraphs; and Figure 5) and in order to use antibodies that express absolute specificity for unique conformational determinants and therefore may be employed to focus studies of protein structure on individual conformational features (page 495, left column, 1st paragraph, lines 1-8).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Colyer et al with monoclonal antibodies Anti-bSt-1 through Anti-bSt-4, Anti-bSt-7, and Anti-bSt-16 to bovine somatotropin, wherein the six monoclonal antibodies have been characterized and grouped, wherein three of these antibodies (Anti-bSt-1,2, and 3) demonstrate strong reactivity with native AIM-bound bSt but little or no reactivity with conformationally modified bSt, Anti-bSt-4 is capable of recognizing all forms of bSt examined, Anti-bSt-7 binds well to native bSt and to bSt denatured under non-reducing conditions, and Anti-bSt-16 is "conformation-sensitive", as taught by Pfund et al, in order to determine the reactivities of antibodies with native and conformationally modified antigenic species that may be evaluated side-by-side and in order to use antibodies that express absolute specificity for unique conformational determinants and therefore may be employed to focus studies of protein structure on individual conformational features. One of ordinary skill in the art would have reasonable expectation of success in using monoclonal antibodies and sorting the

monoclonal antibodies into functional groups, as taught by Pfund et al, in the method of Colyer et al, since Colyer et al teach a method that includes the step of contacting polypeptide binding partners to immobilized antigens, and monoclonal antibodies are one type of binding partner that can bind to antigens. Colyer et al also teach the step of measuring the association of antibodies to antigens, and the sorting of antibodies into functional groups, as taught by Pfund et al, is one method of measuring the association of different types of antibodies by identifying antibodies that can bind to various antigen derivatives, after structural modification.

Concerning step (e) of claim 17, the specification does not provide a definition for the term "sorting", as stated above in the rejection supra based on 35 USC § 112. Since the term "sorting" is broad, the Examiner interprets the step to mean the grouping of different mAbs by any means, including non-physical means such as using figures and text to differentiate between different mAbs. Therefore, in the rejection above of this section, Pfund et al reference teaches step (e) by disclosing the grouping of mAbs to bSt in graphical and text format based on the binding profiles of the mAbs to bSt (page 500, right column, 3rd-5th paragraphs; page 501, left column, 1st-2nd paragraphs; and Figure 5).

With regards to claims 18-19, Colyer et al reference teaches that the agents capable of altering the structure of the immobilized antigen are enzymes, wherein the enzymes are chymotrypsin, by disclosing that modification of a polypeptide may include proteolysis (proteolytic cleavage) (page 3, line 20), wherein the proteolytic cleavage is performed by chymotrypsin (page 60, lines 18-21).

With regards to claim 21, Colyer et al reference teaches that the biosensor surface is a Biacore sensor, by disclosing that the solid phase may be a BIAcore chip (page 3, lines 12-15).

18. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Colyer et al (WO 00/50902) in view of Pfund et al (Molecular Immunology 1990, 27(6):495-502) as applied to claim 17 above, and further in view of Lin et al (Journal of Food Science 1976, 41(5):1056-1060).

Colyer et al and Pfund et al references have been disclosed above, but fail to teach that the agent capable of altering the structure of the immobilized antigen is glutaraldehyde.

Lin et al reference teaches chemical modification of a collagen membrane by glutaraldehyde to cross-link the collagen membrane, in order to determine the effect of the chemical modification on the enzyme-binding capacity of the collagen membrane (1057, left column, 6th paragraph, lines 1-3 and 11th paragraph, lines 1-4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Colyer et al and Pfund et al, with chemical modification of a collagen membrane by glutaraldehyde to cross-link the collagen membrane, as taught by Lin et al, in order to determine the effect of the chemical modification on the enzyme-binding capacity of the collagen membrane. One of ordinary skill in the art at the time of the invention would have reasonable expectation of success in using glutaraldehyde to modify the structure of collagen, as taught by Lin et

al, in the method of Colyer et al and Pfund et al, since Colyer et al and Pfund et al teach the structural modification of immobilized proteins using chemicals, and glutaraldehyde is one example of a chemical that can alter the structural conformation of proteins in a layer.

Conclusion

19. No claims are allowed.

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Tal et al (US 5,763,284) teach epitope mapping using biosensor surfaces with monoclonal antibodies.

Altschuh et al (Biochemistry 1992, 31:6298-6304) teach immobilized peptides on a sensor surface with antibody-peptide binding.

Hochleitner et al (Protein Science 2000, 9:487-496) teach epitope extraction and protein-antibody reactions.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

LYL

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